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09/731,660	12/08/2000	Haruhiko Kouhara	038602/1023	1711

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EXAMINER

HUTSON, RICHARD G

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 01/24/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/731,660

Applicant(s)

KOUHARA ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears in the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 2,4-6 and 11-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2,4-6 and 11-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 October 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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### DETAILED ACTION

Applicants amendment of the specification, submission of formal drawings, cancellation of claims 1, 3 and 19 and amendment of claims 2, 4-6, 11 and 13, Paper No. 10, 10/23/2002, is acknowledged. Claims 2, 4-6 and 11-13 are at issue and are present for examination.

Applicants' arguments filed on 10/23/2002, Paper No. 10, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### *Priority*

Applicants amendment of the first page of the specification to indicate that "This application is a divisional of U.S. Serial No. 08/980,523, filed December 1, 1997, now U.S. Patent No. 6,310,181 which is incorporated by reference in its entirety (including any drawings), and claims priority to U.S. Provisional Application 60/032,093" is acknowledged. It is suggested that this be further amended to "...claims priority to U.S. Provisional Application **No. 60/032,093, filed December 12, 1996**", although this may be done by informal examiners amendment at the time of allowance.

***Drawings***

Applicants newly submitted formal drawing has been approved by the Draftsperson.

***Claim Objections***

Claims 1, 2, 4-6 and 11-13 remain objected to because of the following informalities:

Claims 1, 2, 4-6 and 11-13 each recite "FRS2 polypeptide" or depend from a claim which recites "FRS2 polypeptide". It is suggested that the first time in the claims the term "FRS2 polypeptide" is used it be written out in full, followed by the abbreviation in parenthesis.

In response to this previous objection, applicants stated that they amended claim 4 to recite "Fibroblast Growth Factor Receptor Protein Kinase Substrate 2 (FRS2)". Applicants in fact have not amended claim 4 as such (See page 3 of applicants previous response), but applicants version of claim 4 showing changes made does show such a change (See page 12 of applicants previous response).

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 2, 4-6 and 11-13 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection is stated in the previous office action as it applied to claims 1-6, 11-13, and 19.

Applicants have cancelled claims 1, 3 and 19, amended claims 2, 4-6 and 11 and traverse this rejection as it applies to pending claims 2, 4-6 and 11-13 on the basis that applicants amendment of claims 4 and part (c) of claim 11 satisfies the requirements of 35 U.S. § 112, second paragraph. This is not found persuasive, because applicants amendment of claim 4 and part (c) of claim 11 are drawn to the "structural" limitations of a "FRS2 polypeptide encoding target molecule" (claim 4) and the structural relationship of a FRS2 polypeptide to SEQ ID NO: 1 (part (c) of claim 11). Applicants do not define nor does the specification make clear what applicants consider a "FRS2 polypeptide" is.

As stated in the previous office action, applicants teach that FRS2 stands for "Fibroblast Growth Factor Receptor Protein Kinase Substrate 2" and the FRS2 protein/polypeptide preferably has a number of different biological activities (i.e. the ability to regulate growth factor stimulation of cellular differentiation and cellular proliferation by linking stimulated fibroblast growth factor receptor (FGFR) to the Ras/MAPK cascade via the Grb-2/Sos complex and Grb-2 binding activity). The recitation remains indefinite in that while applicants state in the specification they prefer the "FRS2 polypeptide " to have a number of functional activities, it remains unclear

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which of these preferred functional activities are necessary limitations of a "FRS2 polypeptide".

Claim 11 remains indefinite in the following "...nucleic acid molecule comprising a nucleotide sequence that ..." The claim then recites a number of possible properties of the claimed nucleic acid of the format (a)..., (b)..., (c)... through (k). Part (f) recites "is a polypeptide..." It is believed that applicants intent was "**encodes** a polypeptide..." Part (i) recites "the complement of..." It is believed that applicants intent was "**is** the complement of..." Part (k) recites "the complement of..." It is believed that applicants intent was "**is** the complement of..." .

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4-6 and 11-13 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action as it applied to claims 1-6, 11-13, and 19.

Applicants have cancelled claims 1, 3 and 19, amended claims 2, 4-6 and 11 and traverse this rejection as it applies to pending claims 2, 4-6 and 11-13 on the basis that

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applicants amendment of claim 4 and part (c) of claim 11 satisfies the requirements of 35 U.S. § 112, first paragraph. This is not found persuasive, because applicants amendment of claim 4 is drawn to the "structural" limitations of the "nucleic acid target molecule, not to the claimed nucleic acid probe. Claim 11 continues to encompass any possible nucleic acid which encodes any FRS2 polypeptide. Claim 11 part (d) states that the claimed nucleotide sequence must encode a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1, except that it lacks one or more of the segments of amino acids 1-10, 11-152, or 153-508. Therefore the claimed nucleotide sequence may encode a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks **all** of the segments of amino acids 1-10, 11-152, or 153-508. As SEQ ID NO: 1 is only 508 amino acids, the claimed nucleotide sequence which encodes a polypeptide which lacks all of the segments 1-10, 11-152, and 153-508, would therefore encompass any nucleotide sequence which encodes any FRS2 polypeptide with any amino acid sequence.

As stated in the previous office action, applicants specification only provides a single representative species which encodes the FRS2 polypeptide having the amino acid sequence of SEQ ID NO: 1, encompassed by the claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these nucleic acids by any identifying structural or functional characteristics. Given this lack of additional representative species as encompassed by the claims, Applicants have failed

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to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

Claims 2, 4-6 and 11-13 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a FRS2 polypeptide, wherein said FRS2 polypeptide has the amino acid sequence of SEQ ID NO: 1, does not reasonably provide enablement for any nucleic acid encoding any FRS2 polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action as it applied to claims 1-6, 11-13, and 19.

Applicants have cancelled claims 1, 3 and 19, amended claims 2, 4-6 and 11 and traverse this rejection as it applies to pending claims 2, 4-6 and 11-13 on the basis that applicants amendment of claim 4 and part (c) of claim 11 satisfies the requirements of 35 U.S. § 112, first paragraph because a person of ordinary skill in the art would not endure undue experimentation to make a FRS2 polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1, nor a nucleic acid that encodes a FRS2



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polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO: 1. This argument is not found persuasive. Why would it not be an undue burden on one of skill in the art to make a nucleic acid that encodes a FRS2 polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1? There is no teaching that only 10 amino acids of the FRS2 of SEQ ID NO: 1 are sufficient for the recited function and thus the skilled artisan would be required to construct the entire remainder of the molecule necessary for providing said function. The only guidance provided by the specification for doing so is the sequence of SEQ ID NO: 1 which is insufficient for enablement of all structures as many unrelated structures will encode the same function.

Applicants are further reminded that 112 first paragraph requires that applicant disclose to person skilled in the art to which it pertains, or with which it is most nearly connected, to make **and use** the invention commensurate in scope with these claims. Applicants have not taught how to use a nucleic acid that encodes FRS2 polypeptide that applicants have not clearly defined its use (See above 112 second paragraph rejection). Further applicants are reminded that the previous amendment of claim 4, is drawn to the "structural" limitations of the "nucleic acid target molecule", not to the claimed nucleic acid probe and thus fails to provide any limitations of the structure of the claimed probe itself. Claim 11 continues to encompass **any** possible nucleic acid which encodes **any** FRS2 polypeptide (See above discussion regarding claim 11 part (d) above).

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Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any nucleic acid encoding any FRS2 polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4 and 11 remain rejected under 35 U.S.C. 102(b) as being anticipated by Otilie et al. (*Oncogene* Vol 7, No 8: 1625-1630, August 1992).

The rejection is stated in the previous office action as it applied to claims 1, 3, 4 and 11.

Applicants have cancelled claims 1 and 3, amended claims 4 and 11 and traverse this rejection as it applies to pending claims 4 and 11 on the basis that applicants amendment of claim 4 and part (c) of claim 11 renders the instant claims not

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anticipated by Otilie et al. Applicants traverse that claim 4 requires that the nucleic acid molecule encode a FRS2 polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1 and that that only the first 6 amino acids of Otilie et al. and SEQ ID NO: 1 share such sequence homology. Further applicants traverse that the sequence of Otilie et al. does not share 90% sequence identity to the amino acid sequence of SEQ ID NO: 1 as stated in part (c) of claim 11. This is not found persuasive, because applicants amendment of claim 4 is drawn to the structural limitations of the "nucleic acid target molecule", not to the claimed nucleic acid probe. As such, the nucleic acid molecule of Otilie et al. still meets the limitations of the claim, such that it is capable of detecting a nucleic acid target molecule that encodes a FRS2 polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1. This is such, as any nucleic acid molecule would meet the limitations of the claim, given the proper detection (i.e. hybridization) conditions. Claim 11 continues to encompass any possible nucleic acid which encodes any FRS2 polypeptide (See above discussion of claim 11 part (d)). Thus, Otilie et al. continues to anticipate claims 4 and 11.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 2, 4-6 and 11-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (Oncogene, Vol 13, pages 721-729, 1996).

The rejection is stated in the previous office action as it applied to claims 1, 3, 4 and 11.

For the reasons previously stated, it would have been obvious to one of skill in the art at the time of filing to isolate a nucleic acid molecule encoding the SLP proteins of Wang et al. and express the encoded protein by insertion said nucleic acid molecule into any known expression vector, transforming a suitable host cell and culturing said host cell.

Applicants have cancelled claims 1 and 19, amended claims 4 and 11 and traverse this rejection as it applies to pending claims 2, 4-6 and 11-13 on the basis that applicants amendment of claim 4 and part (c) of claim 11 renders the instant claims unobvious by Wang et al. Applicants point out that Wang et al. fails to disclose any sequences for the SNT-like proteins discussed in the paper and that the claims as they currently read require that the prior art share some identity or homology with SEQ ID NO: 1. This argument is not found persuasive on the basis that as discussed above, applicants amendment of claim 4 (claims 5-6 dependent from) is drawn to the "structural" limitations of the "nucleic acid target molecule, not to the claimed nucleic acid probe and any nucleic acid molecule would meet the limitations of the claim, given the proper detection (i.e. hybridization) conditions. Additionally, claim 11 (claims 2, 12 and 13 dependent from) continues to encompass any possible nucleic acid which encodes any FRS2 polypeptide (See claim 11 part (d)).

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapy Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned

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are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read "Richard Hutson", with a horizontal line extending to the right.

Richard Hutson, Ph.D.  
Patent Examiner  
Art Unit 1652  
January 23, 2003